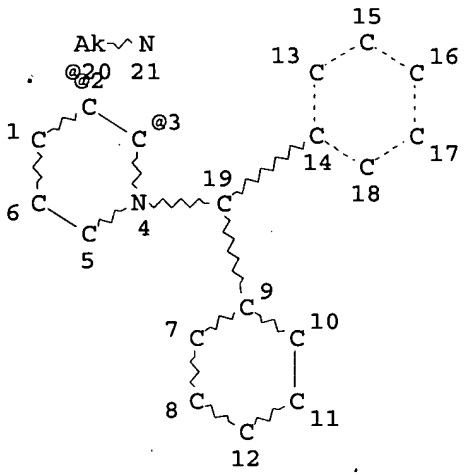
=> d l1
L1 HAS NO ANSWERS
L1 STR



VPA 20-3/2 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 2 14 9
NUMBER OF NODES IS 21

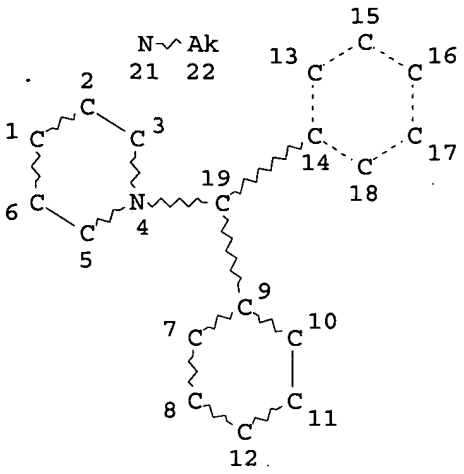
STEREO ATTRIBUTES: NONE

=> s l1 ful
FULL SEARCH INITIATED 12:18:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 46309 TO ITERATE

100.0% PROCESSED 46309 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=> d l6
L6 HAS NO ANSWERS
L6 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 2 14 9
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

=> s l6 ful
FULL SEARCH INITIATED 12:21:12 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 46309 TO ITERATE

100.0% PROCESSED 46309 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

L8 6 SEA SSS FUL L6

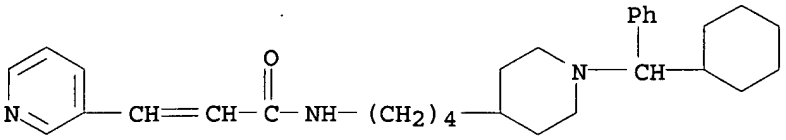
```
=> s l8
L9            8 L8

=> d bib abs hitstr 1-8

L9   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   1999:690954  CAPLUS
DN   131:307106
TI   Use of vitamin PP compounds as cytoprotective agents in chemotherapy
IN   Biedermann, Elfi; Hasmann, Max; Loser, Roland; Rattel, Benno; Reiter,
     Friedemann; Schein, Barbara; Schemainda, Isabel; Seibel, Klaus; Vogt,
     Klaus; Wosikowski, Katja
PA   Klinge Pharma GmbH, Germany
SO   PCT Int. Appl., 145 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   --------
PI   WO 9953920            A1    19991028    WO 1999-EP2686         19990421
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
             JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     DE 19818044            A1    19991028    DE 1998-19818044       19980422
     EP 1031564             A1    20000830    EP 1999-103814         19990226
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     AU 9939282             A1    19991108    AU 1999-39282          19990421
     EP 1079832             A1    20010307    EP 1999-922119         19990421
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
     JP 2002512190          T2    20020423    JP 2000-544324         19990421
     WO 2000050399          A1    20000831    WO 2000-EP1628         20000228
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1154998             A1    20011121    EP 2000-907642         20000228
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2002537380          T2    20021105    JP 2000-600982         20000228
     US 2002160968          A1    20021031    US 2001-935772         20010823
     US 6506572             B2    20030114
PRAI DE 1998-19818044       A     19980422
     EP 1999-103814         A     19990226
     WO 1999-EP2686         W     19990421
     WO 2000-EP1628         W     20000228
OS   MARPAT 131:307106
AB   The invention relates to the use of vitamin PP compds. and/or compds. with
     anti-pellagra activity such as for example nicotinic acid (niacin), and
     nicotinamide (niacin-amide, vitamin PP, vitamin B3) for the reduction,
     elimination or prevention of side-effects of different degrees as well as
     for neutralization of acute side-effects in immunosuppressive or
     cancerostatic chemotherapy or diagnosis, especially with substituted pyridine
     carboxamides, as well as combination medicaments with an amount of compds.
     with vitamin B3 and/or anti-pellagra activity and chemotherapeutic agents
     are especially considered in the mentioned chemotherapies and indications.
```

Nicotinamide at 500 mg/kg twice daily protected mice treated i.p. with antitumor N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide. There were no deaths in the nicotinamide-treated mice and the strong reduction of leukocytes was completely prevented.

IT **201159-48-0**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitamin PP compds. as cytoprotective agents in chemotherapy)

RN 201159-48-0 CAPLUS

CN 2-Propenamide, N-[4-[1-(cyclohexylphenylmethyl)-4-piperidinyl]butyl]-3-(3-pyridinyl)- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:31303 CAPLUS
DN 128:88788
TI Preparation of N-[(azacycloalkyl)alkyl]pyridinealkanamides as antitumor agents and immunosuppressants
IN Biedermann, Elfi; Hasmann, Max; Loser, Roland; Rattel, Benno; Reiter, Friedemann; Schein, Barbara; Seibel, Klaus; Vogt, Klaus
PA Klinge Pharma G.m.b.H., Germany
SO PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9748695	A1	19971224	WO 1997-EP3243	19970620
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	DE 19624704	A1	19980108	DE 1996-19624704	19960620
	ZA 9705439	A	19980223	ZA 1997-5439	19970619
	AU 9733420	A1	19980107	AU 1997-33420	19970620
	EP 934309	A1	19990811	EP 1997-929240	19970620
	EP 934309	B1	20020911		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000512651	T2	20000926	JP 1998-502316	19970620
	AT 223912	E	20020915	AT 1997-929240	19970620
	PT 934309	T	20021231	PT 1997-929240	19970620
	ES 2178779	T3	20030101	ES 1997-929240	19970620
	US 6444823	B1	20020903	US 1998-216075	19981218
	US 2004009967	A1	20040115	US 2002-208656	20020730
	US 2004176605	A1	20040909	US 2003-683509	20031010
PRAI	DE 1996-19624704	A	19960620		
	WO 1997-EP3243	W	19970620		
	US 1998-216075	A1	19981218		
	US 2002-208656	B1	20020730		

OS MARPAT 128:88788

AB R1ZCONR4Z1Z2R2 [I; R1 = (1-oxido)(un)substituted 3-pyridyl; R2 = H, Z3(CH2)r(CR14R15)sR13, COR16, etc.; R4 = H, alkyl, alkoxy, etc.; R13,R14 = H, alkyl, (hetero)aryl, etc.; R15 = H, OH, Me, Ph, CH2Ph; R16 = CF3,

alkoxy, OCH2Ph; Z = cyclopropylene, alkylene which may be interrupted by O, CO, NH, etc.; Z1 = (un)substituted alk(en)ylene, etc.; Z2 = N-attached (un)substituted (ox)azacycloalkylene; Z3 = bond or CO; r = 0-3; s = 0 or 1] were prepared Thus, 4-piperidinebutanol was N-alkylated by Ph2CHBr and the product converted in 2 steps to H2N(CH2)4Z2CHPh2 (Z2 = piperidine-4,1-diyl) which was amidated by 3-pyridinepropionic acid to give R1CH2CH2CONH(CH2)4Z2CHPh2 (R1 = 3-pyridyl, Z2 = piperidine-4,1-diyl). Data for biol. activity of I were given.

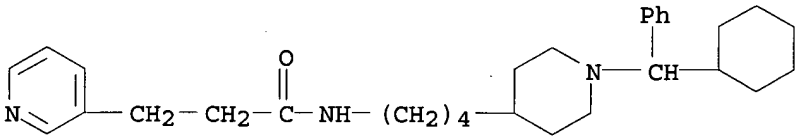
IT **200867-91-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-[(azacycloalkyl)alkyl]pyridinealkanamides as antitumor agents and immunosuppressants)

RN 200867-91-0 CAPLUS

CN 3-Pyridinepropanamide, N-[4-[1-(cyclohexylphenylmethyl)-4-piperidinyl]butyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:28656 CAPLUS

DN 128:102008

TI Preparation and formulation of pyridine derivatives as antitumor agents and immunosuppressants

IN Biedermann, Elfi; Hasmann, Max; Loser, Roland; Rattel, Benno; Reiter, Friedemann; Schein, Barbara; Seibel, Klaus; Vogt, Klaus

PA Klinge Pharma G.m.b.H., Germany

SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2

DT Patent

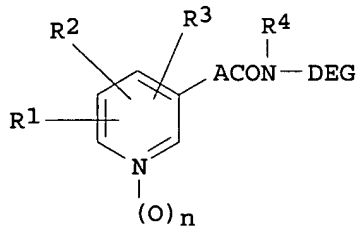
LA English

FAN.CNT 1

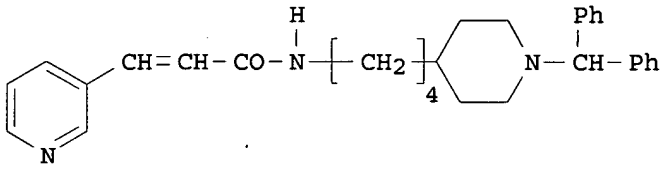
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9748397	A1	19971224	WO 1997-EP3244	19970620
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	DE 19624668	A1	19980219	DE 1996-19624668	19960620
	ZA 9705443	A	19980210	ZA 1997-5443	19970619
	AU 9732624	A1	19980107	AU 1997-32624	19970620
	EP 912176	A1	19990506	EP 1997-928260	19970620
	EP 912176	B1	20020925		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000512652	T2	20000926	JP 1998-502317	19970620
	AT 224713	E	20021015	AT 1997-928260	19970620
	PT 912176	T	20030131	PT 1997-928260	19970620
	ES 2181006	T3	20030216	ES 1997-928260	19970620
	US 6451816	B1	20020917	US 1998-216482	19981218
	US 2004029861	A1	20040212	US 2002-208253	20020730
PRAI	DE 1996-19624668	A	19960620		
	WO 1997-EP3244	W	19970620		
	US 1998-216482	A1	19981218		

OS MARPAT 128:102008

GI



I



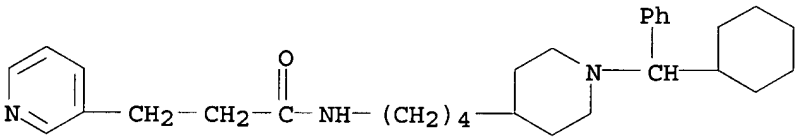
II

AB The title compound I [R1 = H, halo, cyano, etc.; R2 = H, halo, hydroxy, alkyl, etc.; R3 = H, halo, alkyl, etc.; R4 = H, hydroxy, benzyloxy, etc.; n = 0 or 1; A = alkylene, etc.; D = alkylene, etc.; E = piperidine ring (generic structure given), etc.; G = H, etc.] are prepared The title compound II in vitro showed IC50 of 0.008 μM against the WERI-Rb-1 retinoblastoma cells.

IT **200867-91-0P 201159-48-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridine derivs. as antitumor agents and immunosuppressants)

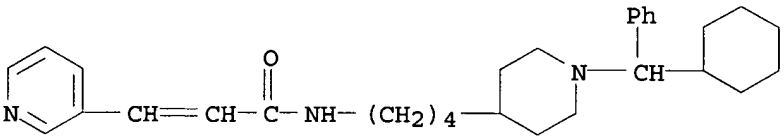
RN 200867-91-0 CAPLUS

CN 3-Pyridinepropanamide, N-[4-[1-(cyclohexylphenylmethyl)-4-piperidinyl]butyl]- (9CI) (CA INDEX NAME)



RN 201159-48-0 CAPLUS

CN 2-Propenamide, N-[4-[1-(cyclohexylphenylmethyl)-4-piperidinyl]butyl]-3-(3-pyridinyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:204606 CAPLUS

DN 116:204606

TI Recording materials using amine compound color-former

IN Sano, Masajiro; Takashima, Masanobu; Satomura, Masato

PA Fuji Photo Film Co., Ltd., Japan

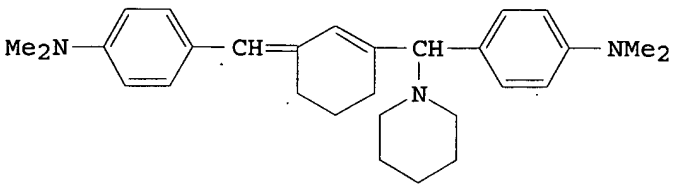
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF

DT Patent

LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 03230991	A2	19911014	JP 1990-25506	19900205
PRAI	JP 1990-25506		19900205		

OS MARPAT 116:204606
GI

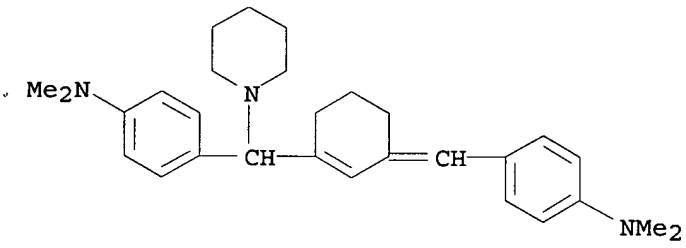


I

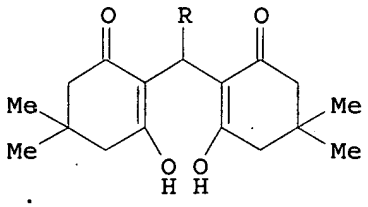
AB The title materials contain, as an electron-donating colorless dye, an amine compound RCR1:CR2CR3:CR4CR5R6R7 [R = R7 = aryl or heterocycle having amine residues; R1-5 = H, monovalent group, R1-5 may form 4- to 12-membered alicyclic rings which may have hetero atoms; R6 = (substituted) amino] and an electron-accepting compound A thermal recording paper using I and bisphenol A showed good storage stability and gave very stable images showing absorption in near IR regions.

IT **140908-42-5P**
RL: PREP (Preparation)
(preparation of, color-former, recording material using)

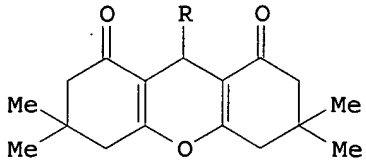
RN 140908-42-5 CAPLUS
CN Benzenamine, 4-[[3-[[4-(dimethylamino)phenyl]methylene]-1-cyclohexen-1-yl]-1-piperidinylmethyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



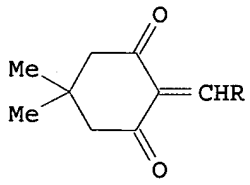
L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:128215 CAPLUS
DN 116:128215
TI Chemistry of dimedone - structures of aldehyde-dimedone adducts
AU Nagarajan, K.; Shenoy, S. J.
CS Res. Cent., Hind. CIBA-GEIGY Ltd., Bombay, 400 063, India
SO Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1992), 31B(2), 73-87
CODEN: IJSBDB; ISSN: 0376-4699
DT Journal
LA English
GI



I



II



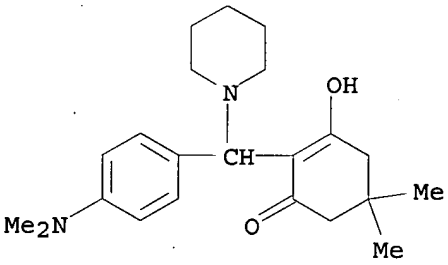
III

AB Dimedone reacted with several aldehydes, e.g., PhCH:CHCHO, PhCHO, 4-Me2NC6H4CHO, in EtOH in a 2:1 ratio of dimedone:aldehyde to give bis adducts, e.g., I (R = PhCH:CH, Ph, 4-Me2NC6H4). Other aldehyde-dimedone adducts, e.g., xanthenes II (R = PhCH:CH, 2,6-Cl2C6H3, 2-thionyl, 2-MeOC6H4) and methylidenedimedones III (R = PhCH:CH, 4-Me2NC6H4CH:CH, 4-N-pyrrolidinylphenyl, etc.) were also prepared

IT **139484-22-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 139484-22-3 CAPLUS

CN 2-Cyclohexen-1-one, 2-[[4-(dimethylamino)phenyl]-1-piperidinylmethyl]-3-hydroxy-5,5-dimethyl- (9CI) (CA INDEX NAME)



L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1983:594812 CAPLUS

DN 99:194812

TI N-(3-Hydroxy-4-piperidinyl)benzamide derivatives

IN Van Daele, Georges

PA Janssen Pharmaceutica N. V., Belg.

SO Eur. Pat. Appl., 137 pp.
CODEN: EPXXDW

DT Patent

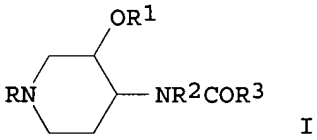
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 76530	A2	19830413	EP 1982-201080	19820903
	EP 76530	A3	19830803		
	EP 76530	B1	19851211		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	CA 1183847	A1	19850312	CA 1982-409480	19820816
	AT 16928	E	19851215	AT 1982-201080	19820903
	SU 1593569	A3	19900915	SU 1982-3489954	19820910
	RO 84704	P	19840717	RO 1982-108663	19820921
	CZ 280009	B6	19950913	CZ 1982-6821	19820923
	SK 278380	B6	19970205	SK 1982-6821	19820923
	DD 203048	A5	19831012	DD 1982-243524	19820927
	DK 8204351	A	19830402	DK 1982-4351	19820930

	DK 165365	B	19921116		
	DK 165365	C	19930405		
	FI 8203348	A	19830402	FI 1982-3348	19820930
	FI 78073	B	19890228		
	FI 78073	C	19890612		
	NO 8203297	A	19830405	NO 1982-3297	19820930
	NO 159378	B	19880912		
	NO 159378	C	19881221		
	AU 8288925	A1	19830414	AU 1982-88925	19820930
	AU 553845	B2	19860731		
	HU 27373	O	19831028	HU 1982-3147	19820930
	HU 189629	B	19860728		
	ES 516131	A1	19831101	ES 1982-516131	19820930
	ZA 8207194	A	19840530	ZA 1982-7194	19820930
	IL 66916	A1	19850929	IL 1982-66916	19820930
	JP 58090552	A2	19830530	JP 1982-171112	19821001
	JP 02045625	B4	19901011		
	PL 138053	B1	19860830	PL 1982-238469	19821001
	PL 138475	B1	19860930	PL 1982-245223	19821001
	ES 542439	A3	19851216	ES 1985-542439	19850422
	US 4962115	A	19901009	US 1989-443060	19891128
	US 5057525	A	19911015	US 1990-535939	19900611
	US 5137896	A	19920811	US 1991-748227	19910820
PRAI	US 1981-307409	A	19811001		
	US 1982-403603	A	19820730		
	EP 1982-201080	A	19820903		
	US 1984-631526	B1	19840718		
	US 1988-258310	B1	19881017		
	US 1989-443060	A3	19891128		
	US 1990-535939	A3	19900611		

GI



I

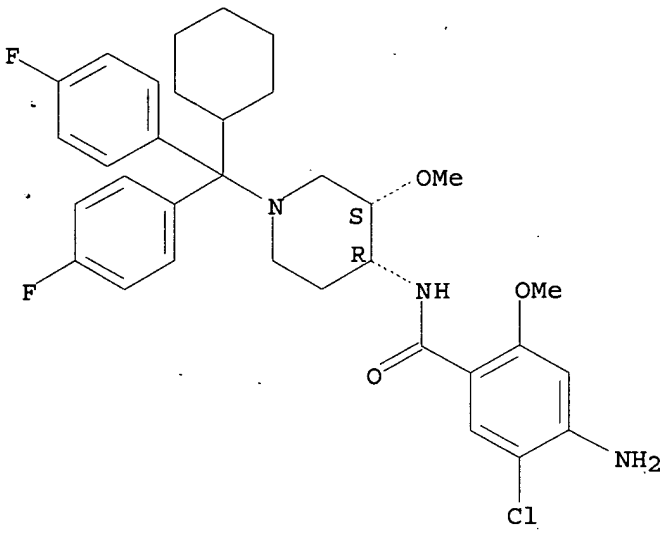
AB Piperidinylbenzamides I [R = alkoxycarbonyl, (un)substituted alkyl, cycloalkyl, aralkyl, etc.; R1 = H, alkyl, aralkyl, aminoalkyl, alkylcarbonyl; R2 = H, alkyl; R3 = (un)substituted Ph] (244 compds.) were prepared Thus, cis-I [R = R2 = H, R1 = Me, R3 = 5,4,2-Cl(H2N)(MeO)C6H2] was treated with 4-FC6H4O(CH2)3Cl to give 42.8% cis-I [R = 4-FC6H4O(CH2)3, R1 = Me, R2 = H, R3 = 5,4,2-Cl(H2N)(MeO)C6H2] (II). II had a min. effective concentration of 0.00016 mg/L for stimulation of contraction of isolated guinea pig ileum.

IT **86719-12-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and gastric motility activity of)

RN 86719-12-2 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-[1-[cyclohexylbis(4-fluorophenyl)methyl]-3-methoxy-4-piperidinyl]-2-methoxy-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1957:43456 CAPLUS
DN 51:43456
OREF 51:8133e-i,8134a-b
TI Aminocyclanols and their products
IN Baltzly, Richard; Lorz, Emil; Russell, Peter B.
PA Burroughs Wellcome & Co. (U.S.A.) Inc.
DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2767185		19561016	US	

GI For diagram(s), see printed CA Issue.

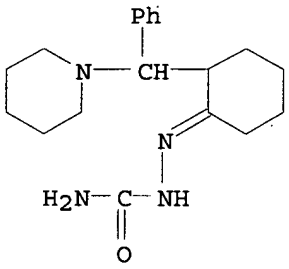
AB A method of preparation is described of PhCH(NR2)CH.CH(OH).(CH2)n where n = 3, 4, or 5, and NR2 is a secondary amino group, either cyclic or noncyclic. To 37.2 g. benzalcyclohexanone and 20 ml. piperidine, 50 ml. ether was added, and the mixture warmed to homogeneity and set aside 5 days. 2-(α-Piperidinobenzyl)cyclohexanone (I) (51 g.) was filtered off, m. 124-5° (from ether-ligroine or EtOAc); semicarbazone, m. 203-5° (decomposition). I (27 g.) reduced with LiAlH4 gave 26 g. epimeric cis- and trans-α-piperidinobenzylcyclohexan-2-ols, as a crude oil. The oil dissolved in hexane kept in the refrigerator deposited 14 g. crystals (A), m. about 90°. The decanted mother liquors yielded on standing 8 g. 2nd crop (B), m. 82-4°. After removal of this crop, the mother liquors were evaporated to half volume and 2 more crops collected, 2 g., m. 82-3° (C), and 1.5 g., m. 110-12° (D). A recrystd. from hexane gave 10 g., m. 110-12°. B and C and the mother liquors of A gave material, m. 82-4°. The recrystd. material from A was identical with D. Further recrystn. failed to raise the m.p. above 111-12°. A total of 10 g. of this isomer was obtained; it formed fine colorless needles. The material from A, B, and C, m. 82-3°, was recrystd. several times without change of m.p.; chromatography on alumina gave 1.2 g. isomer, m. 111-12°, and an isomer, m. 92-3°. Approx. 18-20 g. of the 111° isomer and 7-9 g. of the 92-3° isomer were obtained. Benzalcyclohexanone (37.2 g.) and 20 g. 1-methylpiperazine in absolute ether gave 47 g. 2-[α-(1-methyl-4-piperazinyl)benzyl]cyclohexanone (II), m. 116-17° (from ether-pentane). II and LiAlH4 gave epimeric 2-[α-(1-methyl-4-piperazinyl)benzyl]cyclohexanols, m. 157° and 101°. 2-Benzalcycloheptanone (20 g., m. 45°) and 11 g. 1-methylpiperazine in 15 ml. ether yielded 3 g. 2-[α-(1-methyl-4-piperazinyl)benzyl]cycloheptanone (III), m. 156-7°. III with LiAlH4 gave one epimer of 2-[α-(1-methyl-4-piperazinyl)benzyl]cycloheptanol, m. 144-5° (from etherpentane). Benzalcyclopentanone (43 g.) and 25 g. N-methylpiperazine in 50 ml. ether gave a brown solution but no crystalline product. The crude solution treated with

LiAlH4 yielded the 2 epimers of 2-[α-(1-methyl-4-piperazinyl)benzyl]cyclopentanol, m. 139° and 79-80°. Benzalcyclohexanone was condensed with dimethylamine, morpholine, pyrrolidine, methylbenzylamine, and 1-ethylpiperazine and the uncrystd. amino ketones reduced with LiAlH4 to yield 2-(α-secondary-aminobenzyl)cyclohexanols in 40, 50, 80, 45, and 75% yields, resp. Diethylamine, 2-methylpiperidine, and 1,2,5-trimethylpiperazine, under the same conditions, afforded little or no water-soluble product. Similarly, m-methoxybenzalcyclohexanone and o-chlorobenzalcyclohexanone added methylpiperazine to give the corresponding 2-[α-(1-methylpiperazinyl)benzyl]cyclohexanones, which were reduced to the amino alcs.

IT **102165-91-3**, Cyclohexanone, 2-α-piperidinobenzyl-, semicarbazone
(preparation of)

RN 102165-91-3 CAPLUS

CN Cyclohexanone, 2-α-piperidinobenzyl-, semicarbazone (6CI) (CA INDEX NAME)



L9 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1955:43005 CAPLUS

DN 49:43005

OREF 49:8306a-i,8307a-b

TI The addition of secondary amines to some α-benzal ketones

AU Baltzly, Richard; Lorz, Emil; Russell, Peter B.; Smith, Frances M.

CS Wellcome Research Labs., Tuckahoe, NY

SO Journal of the American Chemical Society (1955), 77, 624-8
CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA Unavailable

OS CASREACT 49:43005

AB cf. following abstract The addition of a number of secondary amines to cyclic and open-chain analogs of benzalcyclohexanone has been studied. In these systems the steric requirements of the amine appear to be quite critical, only cyclic amines and Me secondary amines adding well. The ease of the addition also can be correlated to some extent to recent theories of ring strain. Cycloheptanone (100 g.) and 60 g. BzH added to 20 g. KOH in 350 cc. H2O, the mixture refluxed 3 hrs. and cooled, the oily layer extracted with Et2O, the extract washed with dilute H2SO4 and H2O, dried, and evaporated, and the residue fractionated yielded 100 g. distillate, b0.1 130-5°, which solidified on scratching and recrystd. from pentane to give α-benzalcycloheptanone (I), colorless prisms, m. 45°; semicarbazone, m. 174-5° (decomposition) (from aqueous MeOH). m-MeOC6H4CHO (68 g.) and 150 g. cyclohexanone (II) refluxed 4 hrs. with 25 g. KOH in 500 cc. H2O yielded 50.5 g. m-methoxybenzalcyclohexanone (III), b1.0 160-2°, m. 21-3°. II (95 g.) and 46 g. o-ClC6H4CHO stirred 17 hrs. with 19.8 g. NaOH in 4.55 l. H2O, the solution acidified with approx. 27 cc. AcOH, stirred 6 hrs., and extracted with Et2O, and the extract washed, dried, evaporated, and distilled gave 51 g. o-Cl analog of III, b10 110-20°, pale yellow prisms, m. 70-1° (from pentane). Benzalcyclohexanone (IV) (37.2 g.) and 20 cc. piperidine stirred on a steam bath until homogeneous, the mixture kept at room temperature overnight, and the resulting solid (48 g.) filtered off, washed with pentane, and recrystd. from Et2O-pentane gave 2-(α-piperidinobenzyl)cyclohexanone (V), m. 125-6°; semicarbazone, m. 203-5° (decomposition).

N-Methylpiperazine and IV gave similarly 83% α-(N'-methyl-N-piperazino)benzyl analog (VI) of V, m. 116-17° (from Et2O-pentane). Similarly was prepared over a period of 2 weeks the cycloheptanone analog (VII) of VI, m. 156-7° (from Et2O) in 70-5% yield from benzalcycloheptanone, and the corresponding N'-Et analog of VII, m. 124° (from Et2O). IV did not give an addition product with 2-methylpiperidine but gave adducts with the following compds. (% product given): 1,2,5-trimethylpiperazine 0-3, pyrrolidine 70, Me2NH (in Et2O) 40, PhCH2NHMe 35, Et2NH 1-5. V (5.4 g.) in 50 cc. MeOH containing 1.2 moles AcOH hydrogenated 45 min. over PtO2, the product separated into neutral and basic fractions, and the neutral material (4.0 g.) treated with H2NCONHNH2 gave the semicarbazone of 2-benzylcyclohexanone. VII (13.5 g.) refluxed with 40 g. (iso-PrO)3Al in 300 cc. absolute iso-PrOH until the Me2CO formation ceased, the solvent evaporated, the residue strongly acidified and extracted with Et2O, and the extract worked up gave 8.0 g. 2-benzalcyclohexanol, m. 63°. V (27 g.) in 200 cc. Et2O added during 1 hr. with stirring to 3.8 g. LiAlH4 in 150 cc. Et2O, the mixture refluxed 3-3.5 hrs., cooled, and treated with about 25 cc. H2O, the Et2O solution decanted, the solid residue extracted 3 times with 2N HCl, the acid extract basified, the precipitated oil taken up in Et2O, the solution washed, dried, and evaporated, and the residual crystalline mixture (26 g.) of stereoisomeric alcs. separated into its components gave about 20-5% cis-2-(α-piperidinobenzyl)cyclohexanol, m. 93-4°, and about 75-80% trans-isomer, m. 111-12°. Similarly were prepared the following cycloalkanols (m.p. or b.p./mm. of cis and trans forms, and total yield given): 2-(α-N'-methyl-N-piperazinobenzyl)cyclohexanol (VIII), 154°, 101-2°, 95-100; N'-Et homolog of VIII, 131°, 104°, 60; cycloheptanol analog (IX) of VIII, 103°, 147-8°, 95-100; N'-Et homolog of IX, -, 137°, 95-100°. IV (18.6 g.) warmed with 8.7 g. dry morpholine until homogeneous, the mixture allowed to stand 1 week, dissolved in 100 cc. Et2O, and added dropwise to 3.8 g. LiAlH4 in 150 cc. Et2O, the mixture decomposed in the usual manner the Et2O layer extracted with 2N HCl, washed with H2O, dried and evaporated, the residual pale yellow oil (9.0 g.) scratched to crystallize, and the solid recrystd. from pentane gave 2-benzalcycloheptanol, m. 63°; the acid solution basified and extracted with Et2O, the extract washed with H2O, dried, and evaporated, and the residue distilled, gave 14 g. addition product C17H25NO2, b0.002 100-3°. Similarly were prepared the following compds. (% yield, m.p. or b.p./mm. given): cis-2-(α-N'-methyl-N-piperazino-m-methoxybenzyl)cyclohexanol (X), 60, 163°; o-ClC6H4CH2trans-analog of X, 30,148°; 2-(α-N'-methyl-N-piperazinobenzyl)cyclopentanol, 20, cis 139°, trans 80°; 2-(α-N-morpholinobenzyl)cyclohexanol (XI), 50, 100-3°/0.1; pyrrolidinobenzyl analog, 70, 90-3°/0.2; dimethylaminobenzyl analog of XI, 40, 75-80°/0.2; benzylmethylaminobenzyl analog of XI, 35, 100-5°/0.2; 4-phenyl-4-N-piperidinobutan-2-ol (XII), 73, 65-70°/0.2; 2,2-dimethylpentan-3-ol analog of XII, 64, 78-80°/0.2; 2-methylpentan-3-ol analog of XII, 66, 75-80°/0.2.

IT **102165-91-3**, Piperidine, 1-(α-2-oxocyclohexylbenzyl)-, semicarbazone
(preparation of)

RN 102165-91-3 CAPLUS

CN Cyclohexanone, 2-α-piperidinobenzyl-, semicarbazone (6CI) (CA INDEX NAME)